World Journal of Ophthalmology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.5318/wjo.v4.i2.21

World J Ophthalmol 2014 May 12; 4(2): 21-24
ISSN 2218-6239 (online)
© 2014 Baishideng Publishing Group Inc. All rights reserved.

RETROSPECTIVE STUDY

Presenting clinical features of patients with vitreoretinal lymphoma

Katie M Keck, David J Wilson, Eric B Suhler, Alison Skalet, Christina J Flaxel

Katie M Keck, David J Wilson, Eric B Suhler, Alison Skalet, Christina J Flaxel, Department of Ophthalmology, Casey Eye Institute, Oregon Health and Science University, Portland, OR 97239, United States
Eric B Suhler, Ophthalmology Service, Portland VA Medical Center, Portland, OR 97239, United States
Author contributions: Keck KM carried out data collection, data analysis and drafted the manuscript; Flaxel CJ also carried out data collection; Wilson DJ, Suhler EB, Skalet A and Flaxel CJ were treating physicians and also carried out the correction of the manuscript; all authors read and approved the final manuscript.
Supported by Unrestricted departmental funding from Research to Prevent Blindness (New York, NY)
Correspondence to: Christina J Flaxel, MD, Department of Ophthalmology, Casey Eye Institute, Oregon Health and Science University, 3375 SW Terwilliger Blvd, Portland, OR 97239, United States. flaxelc@ohsu.edu
Telephone: +1-503-4183352 Fax: +1-503-4183352
Received: December 9, 2013 Revised: February 24, 2014
Accepted: April 3, 2014
Published online: May 12, 2014

Abstract

AIM: To assess the presenting clinical features, time from presentation to diagnosis and association with central nervous system (CNS) lymphoma in patients with vitreoretinal lymphoma.

METHODS: Retrospective case series of patients diagnosed with vitreoretinal lymphoma between 2009 and 2011 at a single center.

RESULTS: Fifteen eyes in 9 patients were included. Common presenting ocular symptoms included blurred vision (78%) and worsening floaters (44%) with an average symptom duration prior to presentation of 88.4 d (range 7-365 d). Common ophthalmic exam findings were vitreous haze (89%) and subretinal lesions (56%). The average time from presentation to diagnosis was 56.3 d (range 16-180 d). All patients were diagnosed with large B-cell lymphoma according to pathology results. Lymphoma was restricted to the eye in 33%, while 67% of patients had CNS involvement. Of the patients with secondary vitreoretinal lymphoma, 67% initially presented with CNS lymphoma while 33% initially presented with vitreoretinal lymphoma. Of the patients with CNS involvement, memory loss (67%) was the most common presenting symptom.

CONCLUSION: Vitreoretinal lymphoma most commonly presents with symptoms of blurred vision and/or worsening floaters and vitreous haze on exam. The average time from presentation to diagnosis may be decreasing with increased awareness among clinicians.

© 2014 Baishideng Publishing Group Inc. All rights reserved.

Key words: Primary vitreoretinal lymphoma; Secondary vitreoretinal lymphoma; Primary central nervous system lymphoma; Primary intraocular lymphoma

Core tip: Vitreoretinal lymphoma is a rare, highly malignant lymphoma that can present a diagnostic challenge to clinicians. This case series was designed to identify presenting clinical features associated with vitreoretinal lymphoma.

Keck KM, Wilson DJ, Suhler EB, Skalet A, Flaxel CJ. Presenting clinical features of patients with vitreoretinal lymphoma. *World J Ophthalmol* 2014; 4(2): 21-24 Available from: URL: http://www.wjgnet.com/2218-6239/full/v4/i2/21.htm DOI: http://dx.doi.org/10.5318/wjo.v4.i2.21

INTRODUCTION

Vitreoretinal lymphoma is a rare, highly malignant non-Hodgkin lymphoma, usually of B-cell origin[1]. It more commonly affects the elderly, with a reported mean age

Table 1 Demographic and clinical features of patients with vitreoretinal lymphoma

Patient No.	Age/gender	Bilateral involvement (Y/N)	Presenting ocular symptoms	Symptom onset (days prior to presentation)	Presenting visual acuity	Exam findings	Time from presentation to diagnosis (d)
1	83 yr/F	N	Cloudy vision	30	20/20	Vitreous cells	120
2	65 yr/F	Y	Worsening floaters and blurred vision	120	20/60	Vitreous cells	17
3	86 yr/F	Y	Worsening floaters and blurred vision	365	CF 1′	Vitreous haze and subretinal lesions	45
4	68 yr/M	Y	Blurred vision	Unable to determine	20/60	Vitreous cells and subretinal lesions	30
5	70 yr/F	Y	Cloudy vision	60	20/40	Vitreous cells	16
6	67 yr/M	N	Worsening floaters and blurred vision	7	20/100	Subretinal lesion	180
7	81 yr/M	Y	Blurred vision	14	20/80	Vitreous cells/ haze	30
8	58 yr/M	Y	Worsening floaters and blurred vision	21	20/150	Vitreous haze and subretinal lesions	45
9	63 yr/M	N	Blurred vision	90	20/400	Vitreous cells and subretinal lesions	24

F/M: Female/Male; Y/N: Yes/No; CF 1′: Counting fingers at 1 foot.

of 50-70[1] and is commonly considered to be a localized presentation of primary central nervous system lymphoma[2]. Delays in diagnosis are common given its morphologic similarity to vitreous inflammation. There are limited published series reporting the presenting clinical features of vitreoretinal lymphoma[3-7]. The purpose of this study is to assess the presenting clinical features including initial symptoms, symptom duration, visual acuity, exam findings, and time from presentation to diagnosis in patients diagnosed with vitreoretinal lymphoma.

MATERIALS AND METHODS

Approval for this single-center retrospective case series was obtained from the Institutional Review Board at Oregon Health and Sciences University. Patients were identified through pathology records between January 2009 and December 2011 at the Casey Eye Institute, Oregon Health and Science University. Inclusion criteria were a diagnosis of vitreoretinal lymphoma by vitreous aspirate or diagnostic vitrectomy. Nine patients met the inclusion criteria. The medical records of all 9 patients were extensively reviewed from January 2009 through May 2012.

Patient demographics including gender and age at diagnosis were assessed. Outcome measures assessed included presenting ocular symptoms, symptom duration, presenting visual acuity, ophthalmological exam findings, bilateral involvement at presentation, time from presentation to diagnosis, association with central nervous system (CNS) lymphoma and presenting CNS symptoms.

RESULTS

Fifteen eyes in 9 patients diagnosed with vitreoretinal lymphoma by vitreous aspirate or diagnostic vitrectomy were included. The median observation period was 18 mo (range 4-28 mo). Demographic and clinical features of the patients are summarized in Table 1. Of the 9 patients, 5 were male and 4 were female. The median age at diagnosis was 68 years (range 58-86 years). Presenting ocular symptoms included blurred vision in 7 patients (78%), worsening floaters in 4 patients (44%), and cloudy vision in 2 patients (22%). All 4 of the patients with worsening floaters also reported blurred vision. The median symptom duration prior to presentation was 45 d (range 7-365 d). Best corrected visual acuity at presentation ranged widely among the cohort. One patient (11%) presented with no visual impairment (visual acuity of 20/20). Three patients (33%) had mild visual impairment with a visual acuity of 20/30 to 20/60, 3 patients (33%) had moderate visual impairment with a visual acuity of 20/70 to 20/160 and 2 patients (22%) had severe visual impairment with a visual acuity of 20/200 or worse. Ophthalmic exam findings included vitreous cells/haze in 8 patients (89%) and subretinal lesions in 5 patients (56%). Four patients (44%) had vitreous haze and subretinal lesions on exam. Exam findings were bilateral at presentation in 6 patients (67%). The median time from presentation to diagnosis was 30 d (range 16-180 d).

Association with CNS lymphoma

All patients were diagnosed with large B-cell lymphoma according to pathology results. Of 9 patients, 4 patients (44%) had a history of CNS lymphoma and developed secondary vitreoretinal lymphoma. All 4 patients were treated for CNS lymphoma with one patient receiving whole brain radiation, 3 patients receiving chemotherapy, and one patient undergoing surgery. Of the 3 patients receiving chemotherapy, 2 were treated with methotrexate. At the time of vitreoretinal lymphoma diagnosis, 3 of the 4 patients were free of CNS disease. The time from CNS lymphoma remission to diagnosis of vitreoretinal lymphoma ranged from 9-36 mo. Two patients (22%) developed CNS lymphoma subsequent to the diagnosis of primary vitreoretinal lymphoma (PVRL). One patient was treated with intravitreal methotrexate and rituximab while

the other patient deferred treatment. The time from diagnosis of PVRL to diagnosis of CNS disease ranged from 3-7 mo. Three patients (33%) had PVRL without CNS involvement at the end of the study period with duration of follow-up after diagnosis of PVRL ranging from 8-29 mo. Of 6 patients with CNS lymphoma, presenting CNS symptoms included memory loss in 4 patients (67%), speech problems in 2 patients (33%), difficulty walking in 1 patient (17%), and generalized seizure in 1 patient (17%). All 6 patients were diagnosed with CNS lymphoma by magnetic resonance imaging.

DISCUSSION

Vitreoretinal lymphoma is a rare, highly malignant lymphoma that can present a diagnostic challenge to clinicians. This case series was designed to identify presenting clinical features associated with vitreoretinal lymphoma. In our cohort of 9 patients, the median age at diagnosis of vitreoretinal lymphoma was 68 years with all patients > 50 years of age at diagnosis. This is consistent with previous reports that vitreoretinal lymphoma most commonly affects the elderly[1,3-7]. 56% of patients in our cohort were male. Some previous studies have suggested a female predominance[1,3-5] while others have not[6,7]. The percentage of patients with bilateral involvement at presentation was 67%, which is within the previously reported range of 60%-90%[1,3]. The most common presenting ocular symptom was blurred vision in 7 patients (78%). Additionally, vitreous cells/haze was the most common ophthalmic finding, present in 8 patients (89%). These findings are also consistent with prior published case series[3-7]. Best corrected visual acuity at presentation was highly variable in our cohort, ranging from no visual impairment (visual acuity of 20/20) to severe visual impairment (visual acuity of 20/200 or worse). Wide variation in presenting visual acuities has been reported in a large series by Frenkel *et al*[8].

In the past, delays in the diagnosis of vitreoretinal lymphoma have been common due to its slow onset and ability to imitate other conditions. Most recently, Akpek *et al*[9] reported that the diagnosis can be achieved within 12 mo in 80% of patients. In our series, the median time from presentation to an eye care provider to diagnosis of vitreoretinal lymphoma was 30 d (range 16-180 d). This may indicate an increased awareness by clinicians of the disease. Additionally, in our cohort, 4 of the 9 patients (44%) had a history of CNS lymphoma prior to development of secondary vitreoretinal lymphoma, potentially leading clinicians to suspect the diagnosis earlier in these patients given the known association. However, among the 5 patients who presented with PVRL and no history of CNS lymphoma, the median time from presentation to diagnosis only slightly increased to 45 d (range 30-180 d). Two of the 5 patients (40%) with PVRL subsequently developed CNS involvement during our study period. According to Coupland *et al*[1], 65%-90% of patients presenting with PVRL will go on to develop CNS involvement. Our percentage may be lower given the brief duration of our study period. It is possible that our patients diagnosed with PVRL will develop CNS involvement in the future.

Our study has several limitations, including the retrospective nature of the data, the small number of patients and the brief study period. We chose to limit our study period to the prior 3.5 years (January 2009-May 2012) because we had comprehensive medical records of all patients during this time period. In the future, it will be interesting to evaluate treatment response, visual outcomes and survival rates over a longer time period in similar cohorts of patients.

In conclusion, vitreoretinal lymphoma most commonly presents with symptoms of blurred vision and/or worsening floaters and vitreous haze on exam. Visual acuity is highly variable in the presentation of PVRL. The average time from presentation to diagnosis may be decreasing with increased awareness among clinicians.

ACKNOWLEDGMENTS

EBS is supported by the Department of Veterans' Affairs. The funding organizations had no role in the design or conduct of this research.

COMMENTS

Background

Vitreoretinal lymphoma is a rare, highly malignant lymphoma. It can present a diagnostic challenge to clinicians, given its morphologic similarity to vitreous inflammation. It can develop primarily in the eye or develop in association with central nervous system (CNS) lymphoma.

Research frontiers

There are limited published series reporting the presenting clinical features of vitreoretinal lymphoma. Given the diagnostic challenges associated with vitreoretinal lymphoma, it is important to further distinguish its' presenting features to aid in timely diagnosis.

Innovations and breakthroughs

Recent reports have shown that the diagnosis can be achieved within 12 mo in 80% of patients. In this study, the average time from presentation to diagnosis was even less, suggesting increased awareness among clinicians.

Applications

By further understanding the presenting clinical features of vitreoretinal lymphoma, this study may help aid in more timely diagnosis, contributing to earlier treatment of patients with vitreoretinal lymphoma.

Terminology

Primary vitreoretinal lymphoma, formerly known as primary intraocular lymphoma, is the most common lymphoma affecting the eye, and may go on to affect the CNS. Secondary vitreoretinal lymphoma occurs when patients diagnosed with primary CNS lymphoma develop an ocular manifestation of their lymphoma.

Peer review

Paper is about primary and secondary vitreoretinal lymphoma. Generally well written and informative.

REFERENCES

1 **Coupland SE**, Heimann H, Bechrakis NE. Primary intraocular lymphoma: a review of the clinical, histopathological and molecular biological features. *Graefes Arch Clin Exp Ophthalmol* 2004; **242**: 901-913 [PMID: 15565454 DOI: 10.1007/s00417-004-0973-0]

2 **Chan CC**, Rubenstein JL, Coupland SE, Davis JL, Harbour

JW, Johnston PB, Cassoux N, Touitou V, Smith JR, Batchelor TT, Pulido JS. Primary vitreoretinal lymphoma: a report from an International Primary Central Nervous System Lymphoma Collaborative Group symposium. *Oncologist* 2011; **16**: 1589-1599 [PMID: 22045784 DOI: 10.1634/theoncologist.2011-2010]

3 **Kimura K**, Usui Y, Goto H. Clinical features and diagnostic significance of the intraocular fluid of 217 patients with intraocular lymphoma. *Jpn J Ophthalmol* 2012; **56**: 383-389 [PMID: 22661396 DOI: 10.1007/s10384-012-0150-7]

4 **Grimm SA**, Pulido JS, Jahnke K, Schiff D, Hall AJ, Shenkier TN, Siegal T, Doolittle ND, Batchelor T, Herrlinger U, Neuwelt EA, Laperriere N, Chamberlain MC, Blay JY, Ferreri AJ, Omuro AM, Thiel E, Abrey LE. Primary intraocular lymphoma: an International Primary Central Nervous System Lymphoma Collaborative Group Report. *Ann Oncol* 2007; **18**: 1851-1855 [PMID: 17804469 DOI: 10.1093/annonc/mdm340]

5 **Karma A**, von Willebrand EO, Tommila PV, Paetau AE, Oskala PS, Immonen IJ. Primary intraocular lymphoma: improving the diagnostic procedure. *Ophthalmology* 2007; **114**: 1372-1377 [PMID: 17324466 DOI: 10.1016/j.ophtha.2006.11.009]

6 **Jahnke K**, Korfel A, Komm J, Bechrakis NE, Stein H, Thiel E, Coupland SE. Intraocular lymphoma 2000-2005: results of a retrospective multicentre trial. *Graefes Arch Clin Exp Ophthalmol* 2006; **244**: 663-669 [PMID: 16228920 DOI: 10.1007/s00417-005-0138-9]

7 **Hoffman PM**, McKelvie P, Hall AJ, Stawell RJ, Santamaria JD. Intraocular lymphoma: a series of 14 patients with clinicopathological features and treatment outcomes. *Eye* (Lond) 2003; **17**: 513-521 [PMID: 12802353 DOI: 10.1038/sj.eye.6700378]

8 **Frenkel S**, Hendler K, Siegal T, Shalom E, Pe'er J. Intravitreal methotrexate for treating vitreoretinal lymphoma: 10 years of experience. *Br J Ophthalmol* 2008; **92**: 383-388 [PMID: 18303160 DOI: 10.1136/bjo.2007.127928]

9 **Akpek EK**, Ahmed I, Hochberg FH, Soheilian M, Dryja TP, Jakobiec FA, Foster CS. Intraocular-central nervous system lymphoma: clinical features, diagnosis, and outcomes. *Ophthalmology* 1999; **106**: 1805-1810 [PMID: 10485554 DOI: 10.1016/S0161-6420(99)90341-X]

P- Reviewers: Paydas S, Wang YS **S- Editor**: Song XX
L- Editor: A **E- Editor**: Liu SQ

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com

© 2014 Baishideng Publishing Group Inc. All rights reserved.